

Derwent WPI

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WPI Acc No: 1983-49522K/198321

Related WPI Acc No: 1985-191419

XRAM Acc No: C83-048113

**N-aminoacyl-azabicyclooctane carboxylic acid derivs. -
useful as hypotensives, and their intermediates**

Patent Assignee: HOECHST AG (FARH)

Inventor: BECKER R; GEIGER R; SCHOELKENS B; TEETZ V; URBACH H; SCHOLKENS B

Number of Countries: 028 Number of Patents: 056

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
EP 79022	A	19830518	EP 82110070	A	19821102	198321	B
DE 3226768	A	19830526				198322	
AU 8290145	A	19830512				198326	
NO 8203674	A	19830530				198328	
JP 58103364	A	19830620	JP 8290188	A	19821104	198330	
FI 8203757	A	19830630				198332	
DK 8204904	A	19830704				198333	
NO 8301593	A	19830704				198333	
NO 8301594	A	19830704				198333	
ZA 8208085	A	19830719				198347	
ES 8307746	A	19831101				198406	
HU 28389	T	19831228				198406	
ES 8308541	A	19831201				198408	
ES 8308542	A	19831201				198408	
PT 75792	A	19840223				198412	
HU 32077	T	19840628				198430	
CA 1187087	A	19850514				198524	
DD 219480	A	19850306				198527	
DD 203047	A	19831012				198533	
CA 1193607	A	19850917				198542	
CA 1197252	A	19851126				198601	
EP 79022	B	19860312				198611	
DE 3269875	G	19860417				198617	
CS 8207874	A	19860417				198622	
CS 8501045	A	19860417				198622	
JP 61293967	A	19861224	JP 8290187	A	19821104	198706	
JP 62000051	A	19870106				198706	
FI 8603400	A	19860822				198723	
FI 8603401	A	19860822				198723	
AU 8768509	A	19870507				198724	
AU 8768510	A	19870507				198724	
SU 1277895	A	19861215	SU 3679915	A	19831222	198733	
SU 1327787	A	19870730	SU 3513217	A	19821103	198811	
US 4727160	A	19880223	US 84658902	A	19841009	198811	
KR 8900007	B	19890302				198933	
US 4879403	A	19891107	US 88267753	A	19881102	199003	
FI 8905951	A	19891213				199010	
JP 2104526	A	19900417				199021	
JP 2104573	A	19900417				199021	
DE 3280196	G	19900726				199031	
IL 67172	A	19910730				199133	
IL 84056	A	19910730				199133	

IL 84057	A	19910730				199133
JP 91055449	B	19910823				199138
US 5053519	A	19911001	US 89318519	A	19890228	199142
US 5061722	A	19911029	US 89296513	A	19890112	199146
JP 92007741	B	19920212				199210
JP 4217949	A	19920807	JP 8690187	A	19821104	199238
			JP 9177209	A	19821104	
DK 9201144	A	19920917	DK 824904	A	19821104	199252
			DK 921144	A	19920917	
JP 93031544	B	19930512	JP 82192622	A	19821104	199322
DK 166624	B	19930621	DK 824904	A	19821104	199330
JP 93059105	B	19930830	JP 82192622	A	19821104	199337
			JP 8690187	A	19821104	
JP 93065508	B	19930917	JP 82192622	A	19821104	199340
			JP 89207997	A	19821104	
CZ 9104162	A3	19930915	CS 914162	A	19911230	199346
JP 94094443	B2	19941124	JP 8690187	A	19821104	199445
			JP 9177209	A	19821104	
DK 172751	B	19990628	DK 921144	A	19920917	199932

Priority Applications (No Type Date): DE 3226768 A 19820717; DE 3143946 A 19811105

Cited Patents: 6.Jnl.Ref; DE 1955375; EP 37231; JP52039020; JP52116485; No-SR.Pub; 00 4.Jnl.

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
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EP 79022	A	G	37		
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Designated States (Regional): AT BE CH DE FR GB IT LI LU NL SE

EP 79022	B	G			
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Designated States (Regional): AT BE CH DE FR GB IT LI LU NL SE

US 5053519	A		9		
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US 5061722	A		9		
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JP 4217949	A		10	C07C-237/06	Div ex application JP 8690187
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DK 9201144	A			C07D-209/52	Div ex application DK 824904
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JP 93031544	B		6	C07D-209/52	Based on patent JP 58103364
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DK 166624	B			C07K-005/06	Previous Publ. patent DK 8204904
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JP 93059105	B		11	C07D-209/52	Div ex application JP 82192622
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					Based on patent JP 62000051
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JP 93065508	B		7	C07D-209/52	Div ex application JP 82192622
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					Based on patent JP 2104573
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JP 94094443	B2		10	C07C-227/08	Div ex application JP 8690187
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					Based on patent JP 4217949
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DK 172751	B			C07D-209/52	Previous Publ. patent DK 9201144
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CZ 9104162	A3			C07D-209/52	
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Abstract (Basic): EP 79022 A

Azabicyclooctane derivs. of formula (I) and their physiologically acceptable salts are new: (Hydrogen atoms at ring positions 1 and 5 are cis to each other and the 3-carboxy gp. has the endo orientation. R1 is H, allyl, vinyl or the side chain of an opt. protected naturally occurring alpha-amino acid. R2 is H, 1-6C alkyl, 2-6C alkenyl or aryl (1-4C alkyl). Y is H or hydroxy and Z is H, or Y and Z are together oxygen. X is 1-6C alkyl, 2-6C alkenyl, 5-9C cycloalkyl, 6-12C aryl (opt. substd. 1-3 times by 1-4C alkyl or alkoxy, hydroxy, halo, nitro, amino (opt. substd. by 1 or 2 1-4C alkyl), or methylenedioxy) or indol-3-yl).

Also new are the intermediates (IIIa) and (IIIb), and their salts,

(W is H, 1-6C alkyl or 7-8C aralkyl; W' is a gp. removable by hydrogenolysis, acid or base; and R2 is not benzyl or p-nitrobenzyl if W' is benzyl).

(I) have a strong and long-lasting hypotensive action (by inhibition of angiotensin-converting enzyme). Unit doses usually contain 1-100 mg.

Abstract (Equivalent): EP 79022 B

Azabicyclooctane derivs. of formula (I) and their physiologically acceptable salts are new: (Hydrogen atoms at ring positions 1 and 5 are cis to each other and the 3-carboxy gp. has the endo orientation. R1 is H, allyl, vinyl or the side chain of an opt. protected naturally occurring alpha-amino acid. R2 is H, 1-6C alkyl, 2-6C alkenyl or aryl (1-4C alkyl). Y is H or hydroxy and Z is H, or Y and Z are together oxygen. X is 1-6C alkyl, 2-6C alkenyl, 5-9C cycloalkyl, 6-12C aryl (opt. substd. 1-3 times by 1-4C alkyl or alkoxy, hydroxy, halo, nitro, amino (opt. substd. by 1 or 2 1-4C alkyl), or methylenedioxy) or indol-3-yl).

Also new are the intermediates (IIIa) and (IIIb), and their salts, (W is H, 1-6C alkyl or 7-8C aralkyl; W' is a gp. removable by hydrogenolysis, acid or base; and R2 is not benzyl or p-nitrobenzyl if W' is benzyl).

(I) have a strong and long-lasting hypotensive action (by inhibition of angiotensin-converting enzyme). Unit doses usually contain 1-100 mg. (37pp)

Abstract (Equivalent): US 5061722 A

Cis-endo-2-azabicyclo- (3.3.0)-octane-3-carboxylic acids of formula (I) and their salts are new. R2 = H, CH3, C2H5 or benzyl. The H atoms on the ring C atoms in the 1- and 5-posns. are in the cis configuration w.r.t. each other, the CO2H gp. on ring C atom in the 3-posn. is in the endo posn. w.r.t. the bicyclic ring system and the chirality centres all have the S-configuration.

N-(1-S-carboethoxy-3-phenyl-propyl)-S-alanyl-cis-endo-2-azabicyclo- (3.3.0)-octane-3-S-carboxylic acid is specifically claimed.

USE - As hypotensives (claimed).

US 5053519 A

A mixt. of enantiomers of cis-endo-2-azabicyclo (3.3.0) octane -3-carboxylic acid esters of formula (Ia) and (Ib) or their salts with acids or bases is new. In the formulae, W = H, 1-6C alkyl or 7-8C aralkyl. (Ia) and (Ib) may be prepared from cyclopentanone enamines of formula (II) and N-acylated beta-halo-alpha-amino carboxylic acid esters of formula (III). In (II) X1 = 2-10C dialkylamino or gp. (IV) where m and p = 1-3 and m+p = 3 or more and A = CH2, NH, O or S. In (III) X2 = a nucleofugic gp., e.g. Cl or Br, Y1 = 1-5C alkanoyl, 7-9C aroyl or another protective gp. customary in peptide chemistry which can be split off under acid conditions and R2 = 1-5C alkyl or 7-9C aralkyl.

USE - As intermediates for cis, endoazabicyclo (3.3.0) octane carboxylic acids useful as hypotensive agents. (9pp)c

US 4879403 A

A cpd. X-CO-CH2-C'H(COOR')-NH-C'H(R)-COOQ is produced by reacting an S-alpha-amino acid ester H2N-C'H(R)-COOQ with a keto-acrylic acid ester X-CO-CH=CH-COOR' to obtain a mixt contg mainly the desired cpd, isolating the desired cpd. by crystallisation and pref. removing Q by hydrogenolysis.

In the formulae the chiral centres C' have the S configuration; R is Me or 4-amino-butyl both opt. acylated; R' is 1-6C alkyl, pref. Me

or Et; X is R', 2-6C alkenyl, 5-9C cycloalkyl or 6-12C aryl all opt 1-3 times substd. by 1-4C alkyl or alkoxy or alkylamino, OH, halogen, NO₂, NH₂, di(1-4C) alkylamino and/or methylenedioxy or is indole-3-yl; Q is an esterifying gp removable by hydrogenolysis. X is esp Ph opt. 1-2 times substd. by F and/or Cl.

USE/ADVANTAGE - Used to control high blood pressure; the cpd. has a long lasting, intense hypotensive action and can be given orally or perenterally. (9pp),

US 4727160 A

New cis, endo-2-azabicyclo(3,3,0)-octane-3- carboxylic acid esters of formulae (IIIa) and (IIIb) and salts, can be made by new process comprising cyclising (X) to intermediate (XIa) and (XIb) and catalytic hydrogenation or redn. (X) are obt'd. by reacting cyclopentanone enamine (VI), or radical (VII) and N-acylated beta-halogeno-alpha amino carboxylic acid esters (VIII). W is H, 1-6C alkyl, 7-8C aralkyl; Y is 1-5C alkanoyl, 7-9C aroyl; R₂ is 1-5C alkyl, 7-9C aralkyl, X₁ is 2-10C dialkylamino or (A) where m and o are each 1-3; (m + o) is 3; A is CH₂, NH, O or S; X₂ is Cl, Br or acrylic acid (B).

USE - Intermediate to cis, endoazabicyclo(3,3,0)-octane carboxylic acid of formula (I) by reacting (II) with (IIIa) or (IIIb). R₁ is H, vinyl, allyl, or side chain of alpha amino acid R₁-CH(NH₂)COOH. Y is H or OH; Z is H, or Y and Z together are O; X is 1-6C alkyl, 2-6C alkenyl, 5-9C cycloalkyl 6-12C aryl, opt. substd. (I) are ACE-inhibitors used as long-lasting hypotensives at dosages eg. 13-1300 (13-400) mcg/kg/day p.o. Low toxicity. (9pp)

Title Terms: N; AMINO; ACYL; AZA; BI; CYCLOOCTANE; CARBOXYLIC; ACID; DERIVATIVE; USEFUL; HYPOTENSIVE; INTERMEDIATE

Derwent Class: B02

International Patent Class (Main): C07C-227/08; C07C-237/06; C07D-209/52; C07K-005/06

International Patent Class (Additional): A61K-031/40; A61K-031/405; A61K-037/02; C07C-099/00; C07C-101/28; C07C-103/52; C07C-227/10; C07C-227/14; C07C-227/16; C07C-229/28; C07C-229/36; C07D-029/02; C07D-317/48; C07D-317/60; C07D-403/12; C07D-405/12; C07D-451/04; C07K-001/02; C07K-005/12

File Segment: CPI

Manual Codes (CPI/A-N): B06-A02; B06-D01; B06-D04; B10-B02B; B12-F05; B12-G01; N05-C

Chemical Fragment Codes (M2):

01 D011 D013 D019 D020 D021 D022 D140 D601 D690 D699 F014 F521 G002
G010 G011 G012 G013 G014 G015 G016 G017 G019 G030 G040 G050 G100
G111 G112 G553 G563 G573 G583 H1 H100 H101 H102 H103 H141 H142 H143
H181 H182 H2 H211 H341 H342 H343 H401 H402 H403 H404 H405 H421 H441
H442 H443 H444 H481 H482 H498 H541 H542 H543 H600 H601 H602 H603
H608 H609 H641 H642 H643 H713 H714 H716 H721 H722 H723 J0 J013 J014
J1 J111 J171 J172 J271 J3 J371 J372 J581 L250 L432 M210 M211 M212
M213 M214 M215 M216 M231 M232 M233 M240 M262 M272 M273 M280 M281
M282 M283 M311 M312 M313 M314 M315 M316 M321 M322 M323 M331 M332
M333 M340 M342 M343 M344 M349 M371 M373 M381 M391 M392 M412 M511
M512 M513 M520 M521 M530 M531 M532 M533 M540 M541 M630 M640 M650
M710 M800 M903 P526 P616 V814
02 D012 D690 G010 G100 J0 J011 J111 J211 M210 M211 M212 M213 M214 M215
M216 M231 M232 M233 M272 M280 M281 M311 M312 M320 M321 M331 M332
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03 D011 D019 D020 D021 D022 D140 D601 D699 F014 F521 G002 G010 G011
G012 G013 G014 G015 G016 G017 G019 G030 G040 G050 G100 G111 G112

G113 G553 G563 G573 G583 H1 H100 H101 H102 H103 H141 H142 H143 H181
H182 H341 H342 H343 H401 H402 H403 H404 H441 H442 H443 H444 H481
H498 H541 H542 H543 H600 H601 H602 H603 H608 H609 H641 H642 H643
H714 H721 H722 J0 J012 J013 J171 J172 J2 J271 J272 J371 J5 J581 L250
L432 M210 M211 M212 M213 M214 M215 M216 M231 M232 M233 M240 M262
M272 M273 M280 M281 M282 M283 M311 M312 M313 M314 M315 M321 M322
M331 M332 M333 M340 M342 M343 M344 M349 M371 M373 M381 M391 M392
M412 M413 M414 M415 M416 M510 M511 M512 M520 M521 M530 M531 M532
M533 M540 M541 M620 M710 M903

Ring Index Numbers: 00417; 00446; 00992